

CRA TRAINING

BASIC III

SITE INITIATION

SITE INITIATION VISIT (SIV)

DAN SFERA

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WHAT IS AN SIV?

- What does the ICH/GCP say?
 - ✓ Section 5.23 of the ICH/GCP states that, “For multi-center trials, the sponsor should ensure that...5.23.4: All investigators are given instructions on following the protocol, on complying with a uniform set of standards for the assessment of clinical and laboratory findings, and on completing the CRFs. 5.23.5: Communication between investigators is facilitated.”
- What is the SIV?
 - ✓ The SIV is required to prepare and set up a research site to conduct a study and must occur prior to patient recruitment. The principal investigators (PI) must attend this visit together with as many members of the research team as possible.

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PURPOSE

- The purpose of this meeting is to discuss the clinical protocol, especially the inclusion/exclusion criteria, study procedures, and the research participant pathways. The sponsor prefers that it is at this meeting that discussions about the monitoring plan take place, including discussions about the standard operating procedures (SOPs) and also the requirements of the ICH/GCPs.
- According to the Institute for Clinical Research, "The purpose of this meeting is much the same as for an investigator meeting. It ensures the investigator and the site staff are familiar with study document, investigational medicinal product (if applicable), administrative procedures and that they are aware of the investigator's responsibilities regarding compliance with the clinical protocol and the care of study subjects. The need for an initiation visit is sometimes removed by utilizing the investigator meeting to complete this process."

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WHAT TO DO BEFORE SIV

- Send a Confirmation Letter
- Confirm Time, Date, Attendees
 - ✓ Who's joining you at the visit. It is always advisable that the PI attends this meeting/visit
- What will be discussed at SIV
 - ✓ Protocol
 - ✓ IP (investigational medicinal product)
 - ✓ Safety profile of IP
 - ✓ Reminding the investigators of principal responsibilities of the PI.

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WHAT TO DO BEFORE SIV CONT.

- Take care of some paperwork; make sure you have received and completed the site regulatory packet. Thus everything in the regulatory binder at the site level should have been taken care of and also the trial master file at the sponsor level. Your main work is to make sure that everything is properly filed and completed.

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DURING THE SIV

- Protocol amendments and documented trainings
 - ✓ The study just started except for add-on sites or rescue sites.
 - ✓ Reason for protocol amendments, 1) is that there is an add-on site 2) Maybe the study just started but the sponsor has decided to revise the protocol or amend the protocol; thus ICF is going to be amended as well, most recent version of the protocol and you have to document all of these things; the more documentation you have the better. Documenting the trainings you did for the new protocol and all who attended. The good sites will have done the training and some just don't. Thus you have to make sure that they have done that and document whatever you do.

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DURING THE SIV CONT.

- IP storage and administration: Site must have received their IP (investigational product)
 - ✓ Some sites don't receive it until they have screened their first participant; especially in cases where the IP is not that readily available, thus they prefer to send it to sites that have started screening
 - ✓ Make sure the site has been keeping a temperature log of the IP storage, when did they receive the IP? Are the shipping documents signed by the site coordinator? Checked temperature of the IP during transit? Looking for any temperature excursion. If there was none then the site has to log in the shipment of the IP in the IWRS and then store it in the storage (fridge or room). Always check the recommended temperature range. Any temperature excursion you need to quarantine the IP; that means you set it aside and send it back to the sponsor.
 - ✓ Look for shipping documents in the regulatory binder (This is where your IATA training comes in handy)
 - ✓ Literally you have to check the shipping log and the IP stored in the lab

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DURING THE SIV CONT.

- Lab Kits including storage
 - ✓ Every protocol where a lab kit is required you want to make sure the site has received their lab kits. You are checking to see that the site has enough for screening their targeted number of participants
 - ✓ Want to make sure that the kits are in a lab and well kept
 - ✓ Lab kits and IP from different channels (lab kits from vendor and IP from sponsor or pharmaceutical companies)
 - ✓ Lab kits per visit/how many specified by the protocol, if the protocol says that do lab draws for the first 7 visits

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DURING THE SIV CONT.

- AE's and SAE's of interest: Redundancy though the training on this is usually done at the investigator meetings
- Safety Reporting Procedures
 - ✓ What happens if a subject does have a side-effect or an AE, or an SAE?
 - ✓ Who documents that?
 - ✓ It is the PI's role to determine causality
- SUSARs: Make sure they are in the regulatory binder and train site personnel on how to properly acknowledge SUSAR reports

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DURING THE SIV CONT.

- Informed Consents and Approval: Amendments on protocol always cause changes in ICF, most recent, signed and dated
- IRB Approval: Most recent, updated, signed and dated
- Delegation of duties Log
 - ✓ Experienced sites will have these logs already filled out, but it can happen that they may not do it also. Blank logs need to be completed. Either leave as action item for next visit, or you can spend some time on it. That depends on the experience of the site.
- Protocol training log: Fill this out as your SIV training

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DURING THE SIV CONT.

- Subject Recruitment Objectives and Expectations
 - ✓ How many subjects was their target and how many have they done
 - ✓ Technically sites can start screening after SIV
 - ✓ Sponsor can help with the marketing/to boost enrollment
 - ✓ Make sure they have a plan
- Investigator and Staff Responsibilities
 - ✓ Remind them of their responsibilities
 - ✓ PI can delegate but 100% solely responsible for how the study is conducted at their site, federally mandated (FDA) and also GCP practice

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DURING THE SIV CONT.

- Study milestones: Sponsor expectations on first screen deadline, mid study screen and end study screen numbers
- Source Document Maintenance
 - ✓ Site are required to create their own source document; this is an issue for CRAs since they can vary very much. You want to make sure they have that created
 - ✓ If they have it, is it complete? Is every single data point as per protocol recorded in the source documents?
 - ✓ That they have it locked in SC's room and SC's office locked.
- EDC and IVRS (IWRS) Access: Make sure PI and SC have access to EDC whatever type it is

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DURING THE SIV CONT.

- Monitoring expectations
 - ✓ Let them know your monitoring plan for their site
 - ✓ How you handle queries. Let them know your style, are you an emailing guy, call guy, anyway
- Regulatory
 - ✓ Make sure FDA Form 1572 is complete, signed and dated by the PI. Also, that every regulatory documented is up to date and complete
- Data ownership, publications, and confidentiality
 - ✓ Sponsor initiated trial: data all owned by the sponsor
 - ✓ Investigator initiated trial the PI will have rights to publishing the data
 - ✓ But mostly the first

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AFTER THE SIV

- Can the site screen?
- If so, when will they anticipate first subject?
- If not, why?
- Initiation report: It should be completed by the CRA, signed, and also signed off by the Project Manager. You may also need the Sponsor to review the report before finalization, depending very much on the SOPs for the study. Once the report is finalized, it should be filed in the Trial Master File at the Sponsor level and a copy sent to the site/PI/investigator site file.

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AFTER THE SIV CONT.

- Send the follow-up letter: Thank them for their time, detailing any decisions or issues covered. Make sure copies of this follow-up letter be sent to all appropriate site staff.
- Action items
 - ✓ Anything that is due, still pending
 - ✓ Routine items will not delay screening

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CRA Training:

- ☐ Basic I: GCP for Site Monitors
- ☐ Basic II: Site Selection
- ☐ Basic III: Site Initiation
- ☐ Basic IV: Site Monitoring
- ☐ Basic V: Site Close-out
- ☐ Advanced: I: Source Documents
- ☐ Advanced II: Site Regulatory
- ☐ Advanced III: Protocol Deviations, IP Accountability, Miscellaneous

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